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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,836	03/16/2001	Pierre Broun	MBI-0032	7074

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EXAMINER
DAVIS, KATHARINE F

ART UNIT	PAPER NUMBER
1636	13

DATE MAILED: 05/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,836	BROUN, PIERRE	
	Examin r	Art Unit	
	Katharine F. Davis	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,26 and 33-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26* is/are allowed.

6)☒ Claim(s) *1-18 and 33-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply & Appendix B* .

DETAILED ACTION

This Office Action is in response to the Amendment filed on February 4, 2002. Claims 19-25 and 27-32 have been cancelled. Claims 1-18, 26 and 33-50 are pending in the instant application.

The objection to the specification (with regard to the missing application serial numbers at pages 8 and 9), the objection to claim 14, the rejections of claims 5-9, 13, 15 (with regard to the lack of antecedent basis for the first use of the term "promoter" in the claim)-17, 38-42, 46, 47 and 49-50 under 35 U.S.C. 112, second paragraph are all withdrawn in view of the amendments to the claims and the remarks presented by the Applicant in the Amendment filed on February 4, 2002.

Specification

The substitute Sequence Listing (both paper and computer readable copies) has been entered into the instant application. However four nucleotide sequences at page 18, lines 1, 2, 10 and 11 are not identified with SEQ ID NOS and do not appear to be included in the substitute Sequence Listing filed on February 4, 2002. It is noted that the instant specification is a substitute copy of the entire specification filed on May 2, 2001. The above-mentioned nucleotide sequences were at page 17 of the originally filed specification The four nucleotide sequences at page 18, lines 1, 2, 10 and 11 are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Therefore, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide

Sequence and/or Amino Acid Sequence Disclosures. Applicant must provide a substitute paper copy and a substitute computer readable copy of the Sequence Listing and a statement that the content of the substitute paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office action must include a complete response to the requirement for a new Sequence Listing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pool of test transcription factors wherein said pool comprises up to four transcription factors, does not reasonably provide enablement for a pool of test transcription factors wherein said pool comprises more than four transcription factors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 33-50 are drawn to a method of determining whether two or more members of a pool of test transcription factor polynucleotides are required for expression from a pathway gene promoter, the method comprising introducing into a cell a nucleic acid comprising a promoter of a pathway gene operably linked to a reporter gene and a pool of nucleic acid members comprising test transcription factor polynucleotides and detecting expression from said pathway

gene promoter in the cell, thereby determining whether two or more members of the test transcription factor polynucleotide pool are required for expression from said promoter.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The instant claims are considered to be very broad in that the claimed method is drawn to determining whether any two or more members of a pool of test transcription factor polynucleotides are required for expression from any pathway gene promoter in any cell. The instant claims encompass any transcription factor polynucleotide in any pathway in any cell.

The nature of the invention is a method for identifying synergistic effects of transcription factors on pathway genes.

The skill of those practicing the molecular techniques in transcription factor research is high.

An analysis of the prior art indicates that there is no well-known protocol for identifying which transcription factors from a large pool specifically interact to activate a promoter operably linked to a reporter gene construct wherein the promoter/reporter gene construct and the pool of transcription factor polynucleotides are present together within the same cell. The effectiveness of a new protocol for identifying synergistic effects of transcription factors on pathway genes can not be predicted in the absence of prior documented success of similar protocols.

The goal of the claimed method is to determine whether two or more transcription factors are required for expression from a pathway gene promoter; said method involves introducing into a cell a nucleic acid comprising a promoter of a pathway gene operably linked to a reporter gene and a pool of nucleic acid members comprising test transcription factor polynucleotides and detecting expression from said pathway gene promoter in the cell. If a pool comprising a large number of members is introduced into the cell and a positive signal (expression of the reporter gene in the cell) is obtained indicating expression from the pathway gene promoter, which member or members of the pool are binding to the promoter? Is a single member binding or is more than one binding? Although the instant specification describes the method on pages 15-16 little direction or guidance is provided for answering the above questions. The working example (example 2, pages 20-21) involves a pool comprising four transcription factor constructs. No experiments are described wherein the pool comprises more than four transcription factor polynucloetide members.

To attempt to practice the invention one of skill in the art would turn to the specification or the prior art for guidance in practicing the invention. As set forth above, however, the specification and the prior art lack sufficient guidance for practicing the invention. In order to practice the claimed invention one of skill in the art would need to know how to identify which member and/or members of a large pool of transcription factor polynucleotides is binding to the promoter to activate the reporter gene expression and would further need to discern whether the reporter gene expression is caused by a single transcription factor binding or is caused by multiple factors binding to the promoter. Since neither the instant specification nor the prior art

provides answers to these questions one of skill in the art would resort to experimentation in order to practice the claimed invention with no true expectation of a measure of success.

Based on the broad scope of the claims, the nature of the invention, the skill of those in the art, the unpredictability of the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to use the claimed method to determine whether two or more members of a large pool (consisting of more than four members) of test transcription factor polynucloetides are required for expression from a pathway gene promoter. Therefore, the instant invention is not enabled for the full scope of its intended use.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 48 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "high-value" in claims 15 and 48 is a relative term which renders the claim indefinite. The term "high-value" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what metabolites are encompassed by the term "high-value".

The arguments presented by the Applicant at pages 5 and 6 of the Amendment filed on February 4, 2002 have been carefully considered but have not been found to be persuasive.

Applicant refers to the definition of "high-value secondary metabolites" at page 5 of the instant specification which states that "high-value secondary metabolites" are those secondary metabolites that have valuable commercial applications. Additionally, applicant asserts that one of ordinary skill in the art would understand this definition. However the specification still does not provide a definition of "high-value" as it does not give a range for ascertaining the requisite degree of value nor does the specification define a valuable commercial application. It remains unclear what metabolites are encompassed by the term "high-value" as what is considered to be high-value changes with the field and/or commercial application. Thus, the term "high-value" in claims 15 and 48 is a relative term which renders the claim indefinite.

For both the reasons above and the reasons made of record in the previous Office Action mailed on December 14, 2001 the rejection of claims 15 and 48 under 35 U.S.C. 112, second paragraph is maintained.

Claims 1-18 and 33-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 5 is missing a phrase or term (reporter gene or promoter of a pathway gene) after the word "said".

Claim 33 recites the term "biosynthetic pathway gene promoter" in line 5. There is insufficient antecedent basis for this term in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim *et al.* (The Plant Journal 11(6):1237-1251 1997, IDS reference). Kim *et al.* teach a method for determining whether a member of a pool of test transcription factor polynucleotides encodes a pathway transcription factor. The method of Kim *et al.* comprises introducing into a yeast cell a nucleic acid comprising a promoter of a pathway gene (carrot Dc3 gene involved in embryogenesis and thus developmental pathways) operably linked to a reporter gene (HIS3 and lacZ) and a pool of nucleic acid members comprising test transcription factor polynucleotides from a plant (sunflower). The method of Kim *et al.* further comprises detecting expression of the reporter gene in the yeast cell thereby identifying members of the sunflower seed nucleic acid pool which bind to the promoter of the carrot Dc3 gene. See article at page 1238, Cloning of carrot Dc3 promoter-binding proteins and experimental procedures page 1248. Claims 1, 10, 11 and 13 read on the methods disclosed by Kim *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* in view of WO 00/46383 (IDS reference). Kim *et al.* is applied as above in the 102(b) rejection. However, Kim *et al.* does not describe a method wherein the pathway gene is a biosynthetic pathway gene nor does Kim *et al.* carry out their method in plant cells. WO 00/46383 describes methods for modulating metabolite biosynthesis in plants by transfection of cells (including plant cells) with transcription factor polynucleotides. The method described by WO 00/46383 is useful for enhancing the biosynthesis of metabolites by modulation of primary metabolite pathway genes for example, anthranilate synthase (page 55, lines 16-23) and secondary metabolite pathway genes for example, terpenoid and alkaloid pathway genes (see abstract). One of ordinary skill in the art would be familiar with plant biosynthetic pathways and would know of several secondary metabolites produced by plants that are useful as food additives (vanillin) and as pharmaceuticals (alkaloids). The method for identification of transcription factors described by Kim *et al.* was known in the art at the time that the instant invention was made. As one of ordinary skill would realize the importance of many plant metabolites to the food and pharmaceutical industries one of ordinary skill would thus be motivated to use the methods described by Kim *et al.* to identify transcription factors involved in

the biosynthesis of metabolite production in plants in order to develop methods for the increase of metabolite production. It would have been obvious to one of ordinary skill in the art at the time that the instant invention was made to use a promoter of a biosynthetic pathway gene in the method disclosed by Kim *et al.* for identification of biosynthetic pathway transcription factors in cells (including plant cells) therefore arriving at the instant invention and thus rendering the instant invention as claimed in claims 5-9 and 12 obvious. Given the teachings of the cited prior art and given the level of skill of the ordinary artisan at the time that the instant invention was made, said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

Claims 1-18 and 33-50 are rejected. Claim 26 is allowable. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katharine F. Davis whose telephone number is (703) 605-1195 with direct desktop RightFax (703) 746-5199. The examiner can normally be reached on Monday-Friday (8:30am-5:00pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications. Any inquiry of a general nature or any inquiry concerning the formalities of this application should be directed to Patent Analyst Tracey Johnson whose telephone number is (703) 305-2982.

Katharine F. Davis
May 3, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

09/810836 File

Appendix B

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
February 4, 2002	January 15, 2002

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

file

Application No.: 09/810,836

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set by the Office communication to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: Please see attached Office Action under section "Specification"

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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